Amendments to the Specification:

Please amend the first paragraph on page 1 as follows:

This application is a divisional of U.S. Patent Application No. 09/770,834, filed January 25, 2001, now allowed, which claims the benefit of U.S. Provisional Application No. 60/202,466, filed May 8, 2000, the contents of both of which are herewith incorporated by reference.

Please replace the original set of Figures 1-5 with new Figures 1 to 5A-15 attached hereto as **Exhibit 1** (99 pages).

Please enter the Sequence Listing attached hereto as **Exhibit 2** (9 pages) as the Sequence Listing for the subject application.

Please amend the paragraph on page 4, lines 7-19 as follows:

In addition, the invention provides a solution comprising *B. subtilis* ACP having a three dimensional structure defined by the structural coordinates of Figure 5 and 5A-1 to 5A-15, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å. Also provided by the invention is any active site of *B. subtilis* ACP that is defined by the structural coordinates of Figure 5 and 5A-1 to 5A-15, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å. Further, the present invention provides a method for identifying an agent that interacts with any active site of *B. subtilis* ACP, comprising the steps of determining a putative active site of ACP from a three dimensional model of the ACP, and performing various computer fitting analyses to identify an agent which interacts with the putative active site. Again, such agents may act as inhibitors or activators of ACP activity, as

determined by obtaining the identified agent, contacting the same with ACP, and measuring the agent's effect on ACP activity.

Please amend the paragraph on page 4, line 20 through page 5, line 12, as follows:

Yet another aspect of the present invention is a method for identifying an activator or inhibitor of any molecule or molecular complex which comprises an ACP binding site, including any member of the ACPS-like P-pant transferases, comprising the steps of generating a three dimensional model of said molecule or molecular complex using the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 of residues ARG14, MET18, ARG21, GLN22, ARG24, PHE25, ARG28, PHE54, GLU58, ILE68, GLY69, ALA70, SER73 and PHE74 from a first monomer of ACPS, and residue ARG45 from a second monomer of ACPS, or additionally, of residues ASP8, ILE9, THR10, GLU11, LEU12, ILE15, ALA16, SER17, ALA19, GLY20, ALA23, ALA26, GLU27, ILE29, ALA51, LYS57, SER61, LYS62, THR66, GLY67, GLN71, LEU72, GLN75, ASP76, ILE77 and LYS93 from the first monomer of ACPS and residues LEU41, SER42, LYS44, GLU48, GLN83, ASN84, HIS105, THR106 and ALA107 from the second monomer of ACPS, in each case ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, and then selecting or designing a candidate activator or inhibitor that interacts with said molecule or molecular complex using computer fitting analyses of interactions between the three dimensional model of the molecule or molecular complex and the candidate activator or inhibitor. The effect of the candidate activator or inhibitor may be evaluated by obtaining the candidate activator or inhibitor, contacting the same with the molecule or molecular complex, and measuring the effect of the candidate activator or inhibitor on molecular or molecular complex activity.

Please amend the paragraph on page 5, line 13, through page 6, line 2, as follows:

In addition, the present invention provides a method for identifying an activator or inhibitor of any molecule or molecular complex which comprises an ACPS binding site, comprising the steps of generating a three dimensional model of said molecule or molecular complex comprising an ACPS binding site using the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 of residues ARG14, LYS29, ASP35, SER36, LEU37, ASP38, VAL40, GLU41, VAL43, MET44, GLU47, ASP48, ILE54, SER55, ASP56, GLU57 and GLU60, or additionally, of residues ASP13, LEU15, PHE28, GLU30, ASP31, LEU32, GLY33, ALA34, VAL39, LEU42, GLU45, LEU46, GLU49, MET52, GLU53, ASP58, ALA59, and LYS61, in each case ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, and then selecting or designing a candidate activator or inhibitor that interacts with said molecule or molecular complex using computer fitting analyses of interactions between the three dimensional model of the molecule or molecular complex and the candidate activator or inhibitor. The effect of the candidate activator or inhibitor may be evaluated by obtaining the candidate activator or inhibitor, contacting the same with the molecule or molecular complex, and measuring the effect of the candidate activator or inhibitor on molecular or molecular complex activity. Also provided by the present invention are the activators or inhibitors selected or designed using the above-noted methods.

Please amend the paragraph on page 6, lines 13-27, as follows:

In addition, the present invention provides the ACP active site of an ACPS-like P-pant transferase, including, but not limited to, an ACPS, comprising the structural coordinates according to Figure 3 and 3A-1 to 3A-79 of residues ARG14, MET18, ARG21, GLN22, ARG24, PHE25, ARG28, PHE54, GLU58, ILE68, GLY69, ALA70, SER73 and PHE74 from a first monomer of ACPS, and residue ARG45 from a second monomer

of ACPS, in each case ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å. In another embodiment, the active site may include, in addition to the structural coordinates above, the relative the structural coordinates according to Figure 3 and 3A-1 to 3A-79 of residues ASP8, ILE9, THR10, GLU11, LEU12, ILE15, ALA16, SER17, ALA19, GLY20, ALA23, ALA26, GLU27, ILE29, ALA51, LYS57, SER61, LYS62, THR66, GLY67, GLN71, LEU72, GLN75, ASP76. ILE77 and LYS93 from one monomer of ACPS and residues LEU41, SER42, LYS44, GLU48, GLN83, ASN84, HIS105, THR106 and ALA107 from a second monomer of ACPS, in each case ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

Please amend the paragraph on page 6, line 28, through page 7, line 9, as follows:

Finally, the present invention provides the ACPS active site of ACP, comprising the structural coordinates according to Figure 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 of residues ARG14, LYS29, ASP35, SER36, LEU37, ASP38, VAL40, GLU41, VAL43, MET44, GLU47, ASP48, ILE54, SER55, ASP56, GLU57 and GLU60, in each case ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å. In another embodiment, the active site may include, in addition to the structural coordinates above, the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 of residues ASP13, LEU15, PHE28, GLU30, ASP31, LEU32, GLY33, ALA34, VAL39, LEU42, GLU45, LEU46, GLU49, MET52, GLU53, ASP58, ALA59, and LYS61, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

Please amend the paragraph on page 7, lines 11-12, as follows:

Figure 1 depicts the amino acid sequences for the forms of ACP (SEQ ID NO:1) and ACPS (SEQ ID NO:2) used in the growth of ACP/ACPS complex crystals.

Please amend the paragraph on page 7, lines 13-14 as follows:

Figure 2 illustrates the alignment of amino acid sequences for twelve members of the ACPS family, including the consensus sequence. Depicted are amino acid sequences for Aquifex (SEQ ID NO:3), Chlamydophila (SEQ ID NO:4), Helicobacter (SEQ ID NO:5), Staphylococcus (SEQ ID NO:6), Thermotoga (SEQ ID NO:7), Escherichia (SEQ ID NO:8), Rickettsia (SEQ ID NO:9), Streptomyces (SEQ ID NO:10), Treponema (SEQ ID NO:11), Bacillus (SEQ ID NO:12), Bradyrhizobium (SEQ ID NO:13), and Mycobacterium (SEQ ID NO:14).

Please amend the paragraph on page 7, lines 15-25, as follows:

Figure 3 and 3A-1 to 3A-79 provides the atomic structural coordinates for ACPS and ACP as derived by X-ray diffraction of an ACPS-ACP crystal. "Atom type" refers to the atom whose coordinates are being measured. "Residue" refers to the type of residue of which each measured atom is a part - i.e., amino acid, cofactor, ligand or solvent. The "x, y and z" coordinates indicate the Cartesian coordinates of each measured atom's location in the unit cell (Å). "Occ" indicates the occupancy factor. "B" indicates the "B-value", which is a measure of how mobile the atom is in the atomic structure ($Å^2$). "MOL" indicates the segment identification used to uniquely identify each molecule. Under "MOL", "A1", "B1" and "C1" refers to each molecule of ACPS, "AP1", "AP2" and "AP3" refers to each molecule of ACP, and "W" refers to water molecules.

Please amend the paragraph on page 7, lines 26-27 as follows:

Figure 4 represents the sequence alignment of *B. subtilis* ACP, *E. coli* ACP (SEQ ID NO:15), and *Streptomyces coelicolor* A3(2) ACP (SEQ ID NO:16).

Please amend the paragraph on page 8, lines 1-9, as follows:

Figure 5 and 5A-1 to 5A-15 provides the atomic structural coordinates for the restrained minimized mean structure of *B. subtilis* ACP as derived by NMR spectroscopy. "Atom type" refers to the atom whose coordinates are being measured. "Residue" refers to the type of residue of which each measured atom is a part - i.e., amino acid, cofactor, ligand or solvent. The "x, y and z" coordinates indicate the Cartesian coordinates of each measured atom's location (Å). The last column indicates the temperature factor field, representing the rms deviation of the 22 individual NMR structures about the restrained minimized mean structure. All non-protein atoms are listed as HETATM instead of atoms using PDB conventions.

Please amend the paragraph on page 9, lines 3-14, as follows:

"Structural coordinates" are the Cartesian coordinates corresponding to an atom's spatial relationship to other atoms in a molecule or molecular complex. Structural coordinates may be obtained using x-ray crystallography techniques or NMR techniques, or may be derived using molecular replacement analysis or homology modeling. Various software programs allow for the graphical representation of a set of structural coordinates to obtain a three dimensional representation of a molecule or molecular complex. The structural coordinates of the present invention may be modified from the original sets provided in Figures 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 by mathematical manipulation, such as by inversion or integer additions or subtractions. As such, it is recognized that the structural coordinates of the present invention are relative,

and are in no way specifically limited by the actual x, y, z coordinates of Figures 3 and 3A-1 to 3A-79 and Figure 5 and 5A-1 to 5A-15.

Please amend the paragraph on page 9, line 23, through page 10, line 2, as follows:

It will be obvious to the skilled practitioner that the numbering of the amino acid residues in the various isoforms of ACPS, other ACPS-like P-pant transferases and ACP may be different than that set forth herein or may contain certain conservative amino acid substitutions that yield the same three dimensional structures as those defined in Figures 3 and 3A-1 to 3A-79 and Figure 5 and 5A-1 to 5A-15. Corresponding amino acids and conservative substitutions in other isoforms or analogues are easily identified by visual inspection of the relevant amino acid sequences or by using commercially available homology software programs (e.g., MODELLAR, MSI, San Diego, CA).

Please amend the paragraph on page 11, line 17, through page 12, line 12, as follows:

The ACPS protein in the ACPS/ACP complex includes ACPS as well as proteins having ACPS-like P-pant transferase activity, including the consensus sequence shown in Figure 2. More preferably, the ACPS protein or proteins having ACPS-like P-pant transferase activity, comprises the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 for the residues ARG14, MET18, ARG21, GLN22, ARG24, PHE25, ARG28, ARG45, PHE54, GLU58, ILE68, GLY69, ALA70, SER73 and PHE74, or conservative substitutions thereof, and additionally, the residues ASP8, ILE9, THR10, GLU11, LEU12, ILE15, ALA16, SER17, ALA19, GLY20, ALA23, ALA26, GLU27, ILE29, LEU41, SER42, ALA44, GLU48, ALA51, LYS57, SER61, LYS62, THR66, GLY67, GLN71, LEU72, GLN75, ASP76, ILE77, GLN83, ASN84, LYS93, HIS105, THR106 and ALA107, or

conservative substitutions thereof. More particularly, the ACPS protein or proteins having ACPS-like P-pant transferase activity include an ACP binding site defined using the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 of residues ARG14, MET18, ARG21, GLN22, ARG24, PHE25, ARG28, PHE54, GLU58, ILE68, GLY69, ALA70, SER73 and PHE74 from a first monomer of ACPS, and residue ARG45 from a second monomer of ACPS, or additionally including the relative structural coordinates of residues ASP8, ILE9, THR10, GLU11, LEU12, ILE15, ALA16, SER17, ALA19, GLY20, ALA23, ALA26, GLU27, ILE29, ALA51, LYS57, SER61, LYS62, THR66, GLY67, GLN71, LEU72, GLN75, ASP76, ILE77 and LYS93 from the first monomer of ACPS and residues LEU 41, SER42, ALA44, GLU48, GLN83, ASN84, HIS105, THR106 and ALA107 from the second monomer of ACPS. In each case, the ± a root mean square deviation from the backbone atoms of the amino acids is not more than 1.5Å, more preferably not more than 1.0Å, and most preferably, not more than 0.5Å.

Please amend the paragraph on page 12, lines 13-23, as follows:

The ACP protein in the ACPS/ACP complex includes ACP and proteins having ACP activity, and preferably comprises the relative structural coordinates accordingly to Figure 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 for the residues ARG14, LYS29, ASP35, SER36, LEU37, ASP38, VAL40, GLU41, VAL43, MET44, GLU47, ASP48, ILE54, SER55, ASP56, GLU57 and GLU60, or conservative substitutions thereof, and additionally, the residues ASP13, LEU15, PHE28, LYS29, GLU30, ASP31, LEU32, GLY33, ALA34, ASP35, SER36, LEU37, ASP38, VAL39, LEU42, GLU45, LEU46, GLU49, MET52, GLU53, ASP58, ALA59 and LYS61, or conservative substitutions thereof, in each case ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, or more preferably not more than 1.0Å, or most preferably, not more than 0.5Å.

Please amend the paragraph on page 13, line 12, through page 14, line 2, as follows:

The present invention is also directed to an ACP active site of an ACPS-like P-pant transferase, including the active site of ACPS, and comprising the structural coordinates according to Figure 3 and 3A-1 to 3A-79 of residues ARG14, MET18, ARG21, GLN22, ARG24, PHE25, ARG28, PHE54, GLU58, ILE68, GLY69, ALA70, SER73 and PHE74 from one monomer of ACPS, and residue ARG45 from a second monomer of ACPS, in each case ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, or more preferably not more than 1.0Å, or most preferably, not more than 0.5Å. Alternatively, the active site may include, in addition to the structural coordinates define above, the structural coordinates according to Figure 3 and 3A-1 to 3A-79 of residues ASP8, ILE9, THR10, GLU11, LEU12, ILE15, ALA16, SER17, ALA19, GLY20, ALA23, ALA26, GLU27, ILE29, ALA51, LYS57, SER61, LYS62, THR66, GLY67, GLN71, LEU72, GLN75, ASP76, ILE77 and LYS93 from the first monomer of ACPS and residues LEU41, SER42, LYS44, GLU48, GLN83, ASN84, HIS105, THR106 and ALA107 from the second monomer of ACPS, in each case ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, or more preferably not more than 1.0Å, or most preferably, not more than 0.5Å. Preferably, the ACP active site corresponds to the configuration of the ACPS molecule in its state of association or inactivation with an agent, and preferably, ACP.

Please amend the paragraph on page 14, lines 3-17, as follows:

In addition, the present invention provides the ACPS active site of an ACP that comprises the structural coordinates according to Figure 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 of residues ARG14, LYS29, ASP35, SER36, LEU37, ASP38, VAL40, GLU41, VAL43, MET44, SER47, ASP48, ILE54, SER55, ASP56, GLU57 and GLU60, ± a

root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, or more preferably not more than 1.0Å, or most preferably, not more than 0.5Å. Alternatively, the active site further includes, in addition to the coordinates defined above, the structural coordinates according to Figure 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 of residues ASP13, LEU15, PHE28, GLU30, ASP31, LEU32, GLY33, ALA34, VAL39, LEU42, GLU45, LEU46, GLU49, MET52, GLU53, ASP58, ALA59, and LYS61, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, or more preferably not more than 1.0Å, or most preferably, not more than 0.5Å. Preferably, the ACPS active site corresponds to the configuration of the ACP molecule in its state of association or inactivation with an agent, and preferably, ACPS.

Please amend the paragraph on page 16, lines 6-23, as follows:

In this regard, a potential activator or inhibitor of a molecule or molecular complex comprising an ACP binding site, is obtained by (a) generating a three dimensional model of said molecule or molecular complex comprising an ACP binding site using the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 of residues ARG14, MET18, ARG21, GLN22, ARG24, PHE25, ARG28, PHE54, GLU58, ILE68, GLY69, ALA70, SER73 and PHE74 from a first monomer of ACPS, and residue ARG45 from a second monomer of ACPS, and (b) selecting or designing a candidate activator or inhibitor by performing computer fitting analysis of the candidate activator or inhibitor with the three dimensional model generated in step (a). In another embodiment, the relative structural coordinates further include the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 of residues ASP8, ILE9, THR10, GLU11, LEU12, ILE15, ALA16, SER17, ALA19, GLY20, ALA23, ALA26, GLU27, ILE29, ALA51, LYS57, SER61, LYS62, THR66, GLY67, GLN71, LEU72, GLN75, ASP76, ILE77

and LYS93 from said first monomer of ACPS and residues LEU41, SER42, LYS44, GLU48, GLN83, ASN84, HIS105, THR106 and ALA107 from said second monomer of ACPS. In each case, the ± a root mean square deviation from the backbone atoms of the amino acids is not more than 1.5Å, preferably not more than 1.0Å, and most preferably is not more than 0.5Å.

Please amend the paragraph on page 16, line 24, through page 17, line 9, as follows:

A potential activator or inhibitor of a molecule or molecular complex comprising an ACPS binding site, may be obtained by (a) generating a three dimensional model of said molecule or molecular complex comprising an ACPS binding site using the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 of residues ARG14, LYS29, ASP35, SER36, LEU37, ASP38, VAL40, GLU41, VAL43, MET44, GLU47, ASP48, ILE54, SER55, ASP56, GLU57 and GLU60, and (b) selecting or designing a candidate activator or inhibitor by performing computer fitting analysis of the candidate activator or inhibitor with the three dimensional model generated in step (a). In another embodiment, the relative structural coordinates further include the relative structural coordinates according to Figure 3 and 3A-1 to 3A-79 or Figure 5 and 5A-1 to 5A-15 of residues ASP13, LEU15, PHE28, GLU30, ASP31, LEU32, GLY33, ALA34, VAL39, LEU42, GLU45, LEU46, GLU49, MET52, GLU53, ASP58, ALA59, and LYS61. In each case, the ± a root mean square deviation from the backbone atoms of the amino acids is not more than 1.5Å, preferably not more than 1.0Å, and most preferably is not more than 0.5Å.

Please amend the paragraph on page 17, line 10, through page 18, line 2, as follows:

In addition, the invention provides a solution comprising *B. subtilis* ACP having a three dimensional structure defined by the structural coordinates of Figure 5 and 5A-1 to 5A-15, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, more preferably not more than 1.0Å, and most preferably not more than 0.5Å. Also provided by the invention is any active site of *B. subtilis* ACP that is defined by the structural coordinates of Figure 5 and 5A-1 to 5A-15, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, more preferably not more than 1.0Å, and most preferably not more than 0.5Å. In addition, the invention provides a method for identifying an agent that interacts with any active site of *B. subtilis* ACP, comprising the steps of determining a putative active site of ACP from a three dimensional model of the ACP, and performing various computer fitting analyses to identify an agent which interacts with the putative active site. Again, such agents may act as inhibitors or activators of ACP activity, as determined by obtaining the identified agent, contacting the same with ACP, and measuring the agent's effect on ACP activity. In the preferred embodiment, the three dimensional structure of *B. subtilis* ACP is defined by the relative structural coordinates of Figure 5 and 5A-1 to 5A-15, ± a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å, or more preferably not more than 1.0Å, or most preferably, not more than 0.5Å. The use of the NMR solution structure of ACP for the identification of inhibitor binding sites on ACP, for the determination of the solution structure of ACP-inhibitor complexes, and for inhibitor design, is described further below in Examples 3-5.